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# Various mechanisms of myocardial necrosis development due to combat injury as a reason for discussion: a case series

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The real clinical practice of the last 8 years in Ukraine indicates the possibility of myocardial injury developing in wounded with combat trauma, including those meeting the criteria for myocardial infarction (predominantly type 2), which differs significantly in the mechanism of development, resulting in numerous difficulties for doctors in providing medical care to such patients (formulation of the diagnosis, choice of treatment tactics). The current recommendations of the European Society of Cardiology for the management of patients with acute coronary syndromes after the adoption of the Fourth Universal Definition of Myocardial Infarction do not consider special approaches to the treatment of patients with myocardial necrosis associated with trauma.

**The aim** of this publication was to demonstrate, using the example of a case series, the relevance of the problem of terminology, diagnosis, and treatment of myocardial infarction caused by a combat injury.

In all three clinical cases presented, young and middle-aged patients were diagnosed with myocardial infarction in accordance with the Fourth Universal Definition. In all these cases, there were no atherosclerotic coronary artery lesions, and a type 2 myocardial infarction was assumed due to acute myocardial ischemia as a consequence of the injured coronary artery ligation (case 1); microcirculation disorders in the area of myocardial contusion (case 2); anatomical feature of the coronary artery in the form of its intramural course in the presence of severe sympathicotonia and sinus tachycardia (case 3). Because all three patients had myocardial necrosis associated with trauma of the chest and heart, the question arose of the preference for coding such pathology through ICD-10 as section S00-T88 (injury, poisoning and certain other consequences of external causes), namely S26 (injury of heart), but not as I21 (acute myocardial infarction) from the section I00-I99 (diseases of the circulatory system). Thus, the developed pathology in such patients will be clearly associated with the combat trauma, and their treatment will not be tied to the current Ukrainian Unified Protocol for the Management of Patients with ST-segment Elevation Acute Coronary Syndrome.

**Conclusions.** The presented clinical cases substantiate the planning of clinical trials and the development of recommendations for the management of patients with acute myocardial injury (including myocardial necrosis) and trauma of the heart and coronary arteries, depending on the mechanism of damage development.

**Key words:** myocardial infarction, wounds and injuries, heart contusions, heart injuries, myocardial bridging.

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## Різні механізми розвитку некрозу міокарда внаслідок бойової травми як привід для дискусії: серія випадків

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Реальна клінічна практика останніх 8 років в Україні свідчить про можливість розвитку в постраждалих із бойовою травмою уражень міокарда, що відповідають критеріям інфаркту міокарда (переважно 2 типу), але суттєво різняться за механізмом розвитку. Це призводить до низки труднощів для лікарів під час надання медичної допомоги (формулювання діагнозу, вибір тактики лікування). Чинні рекомендації Європейського товариства кардіологів щодо ведення хворих на гострий коронарний синдром після ухвалення Четвертого універсального визначення інфаркту міокарда не розглядають особливих підходів до лікування пацієнтів із некрозом міокарда, що асоційований із травмою.

**Мета роботи –** на прикладі серії випадків показати актуальність проблеми термінології, діагностики та лікування інфаркту міокарда внаслідок бойової травми.

У всіх наведених клінічних спостереженнях пацієнтам молодого та середнього віку встановили діагноз інфаркту міокарда відповідно до Четвертого універсального визначення. У всіх цих випадках атеросклеротичне ураження коронарних судин не виявили, діагностували інфаркт міокарда 2 типу у зв'язку з гострою ішемією міокарда внаслідок лігування травмованої коронарної артерії (випадок 1), порушень мікроциркуляції в зоні забиття міокарда (випадок 2), через особливості розвитку коронарної артерії з інтрамуральним розташуванням на фоні вираженої симпатикотонії з синусовою тахікардією (випадок 3). У зв'язку з наявністю в усіх пацієнтів травми грудної клітки та серця, що передує розвитку некрозу міокарда, виникає питання про кодування такої патології згідно з МКХ-10: радше як S00-T88 (ушкодження, отруєння та деякі інші наслідки зовнішнього впливу), а саме S26 (пошкодження серця), але не як I21 (гострий інфаркт міокарда) з розділу I00-I99 (захворювання системи кровообігу). Так патологія, що розвинулася в цих пацієнтів, буде чітко пов'язана з перенесеною бойовою травмою, а лікування не буде обмежене чинним в Україні Уніфікованим протоколом ведення пацієнтів із гострим коронарним синдромом з підйомом сегмента ST.

**Висновки.** Наведені клінічні випадки обґрунтовують планування клінічних досліджень і розроблення рекомендацій щодо ведення пацієнтів із гострим ураженням міокарда (в тому числі з некрозом міокарда) у хворих із травмою серця та коронарних артерій залежно від механізму розвитку ушкодження.

**Ключові слова:** інфаркт міокарда, поранення та пошкодження, забиття серця, травми серця, міокардіальні містки.

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Because of the war in Ukraine, we received a dramatic experience in treating combat injuries, which revealed the high rate of secondary cardiovascular lesions among servicemen with combat trauma. Such secondary cardiovascular pathology is not a direct consequence of organ damage but developed as a systemic response of the body to damage due to the accompanying dysregulation of the neuroendocrine and autonomic systems [1]. At the same time, there is not enough information in the literature regarding the direct damage to the heart and coronary vessels associated with combat chest trauma, there are no guidelines for the management of acute coronary syndrome caused by trauma, as well as for long-term follow-up and cardiovascular prophylaxis.

Clinical and epidemiological analysis of the nature of combat injuries in 2014–2019 during the Anti-terrorist operation/Operation of the Joint Forces in the East of Ukraine (based on data of 11,964 military personnel) showed that chest injuries rank second after injuries to the limbs in the structure of sanitary losses and account for 10.1 %. Heart, pericardium and large vessels are involved in 10.0–15.0 % cases of penetrating chest injuries, which is accompanied by high mortality (5.1–10.2 %) [2].

In real clinical practice, heart lesions associated with combat chest injuries can not be encoded using existing classifications in some cases. In ICD-10, injuries to the thorax are encoded as S20-29. Section S26 (injury of heart) includes injury of heart with hemopericardium (S26.0) and without it (S26.1), and injury of heart, unspecified with or without hemopericardium (S26.9). Obviously, such a classification does not contribute to the development of optimal strategies for the management of patients with trauma of the heart and coronary vessels. To assess the severity of heart damage, the Abbreviated Injury Scale [3] as well as the Cardiac Injury Organ Scale, proposed in the last century [4], used the classification of myocardial contusion, and blunt cardiac trauma most fully reflects the possible heart damage [5]. This include assessment depending on clinical manifestations, data of additional methods of examination (electrocardiography (ECG), echocardiography (echoCG), blood levels of myocardial necrosis markers, scintigraphy, and radiography), and complications. In the presence of myocardial infarction criteria, clinicians experience difficulties in making a diagnosis, since "myocardial infarction" in accordance with the current ICD-10 is an acute form of coronary heart disease, which dictates the need to treat this condition using protocols for managing acute coronary syndrome, associated with coronary artery disease (as there are no others), which is not suitable for a patient with myocardial necrosis related to trauma, including combat one.

## Aim

The aim of this publication was to demonstrate, using the example of a case series, the relevance of the problem of terminology, diagnosis, and treatment of myocardial infarction caused by a combat injury.

## Clinical case 1

On March 29, 2022, a 21-year-old serviceman, male, received a penetrating gunshot wound to the left half of the chest and left shoulder. He was taken to the nearest medical institution in an extremely severe state within 1 hour after the injury, where a thoracotomy and suturing of the wounds of the left lung, drainage of the left pleural cavity, autotransfusion of blood from the pleural cavity (900 ml of blood), and primary surgical treatment (PST) of the chest and left shoulder wounds were performed as well as metal osteosynthesis of the left humerus with an external fixation device (EFD).

During the PST, it was revealed that the patient had damage to the left anterior descending artery (LAD) in the middle third. To stop the bleeding, the ligation of the damaged vessel was performed; due to the operational situation on the battlefield, the patient was taken to the National M. Amosov Institute of Cardio-Vascular Surgery Affiliated to National Academy of Medical Sciences of Ukraine only the next day.

During a consultation on March 30 at 15:35 (20 hours after the injury), specialists diagnosed using current myocardial infarction criteria Q-myocardial infarction in the region of the anterior-septal-apical-lateral wall of the left ventricle (LV) as a consequence of traumatic damage to the middle third of the LAD.

At 16:00 on the same day, coronary angiography was performed. The coronary conductor was introduced through the right radial artery. It was impossible to separate the ligature of the LAD during staged angioplasty, there were signs of perforation in the ligature zone in the form of myocardial staining without an obvious jet of contrast extravasation (classification type II [6]). Thus, aortocoronary beating heart bypass surgery was performed at 17:00 (CABG) after longitudinal median sternotomy under combined endotracheal anesthesia. The great saphenous vein of the left thigh was used as a shunt (autovenous graft).

Control computed tomography (CT angiography) of the coronary vessels a week after CABG revealed a septoapical LV aneurysm with the presence of 2 thrombi 8 × 4 mm and 11 × 8 mm in size. No evidence of coronary artery narrowing was found: CAD-RADS score (Coronary Artery Disease – Reporting and Data System) 0 (no stenosis)/G (autovenous graft placed). Hypoperfusion of all apical segments as well as anteroseptal and anterior LV segments of mid-cavity section persisted.

In this case, the alertness in terms of the development of myocardial necrosis was explained by the known fact of LAD ligation with the aim to avoid dangerous bleeding after its damage in consequence of the combat trauma. The situation was significantly complicated by the presence of severe posthemorrhagic anemia (hemoglobin level at admission was 70 g/L, at discharge – 95 g/L, red blood cell count was was 2.1 and 2.9 × $10^{12}$/L, respectively). Other possible signs of myocardial necrosis were secondary and non-specific, and could be disguised as the symptoms associated with the combat injury and/or its treatment:

– typical anginal pain was absent, but patient received analgesics, including narcotic ones, due to the presence of a severe concomitant combat injury;

– an increase in the blood levels of myocardial necrosis biomarkers reflected the cytolysis of various tissue cells; it was expectable for such clinical condition with extensive trauma to the soft tissues of the chest and shoulder and reflected not only myocardial damage.

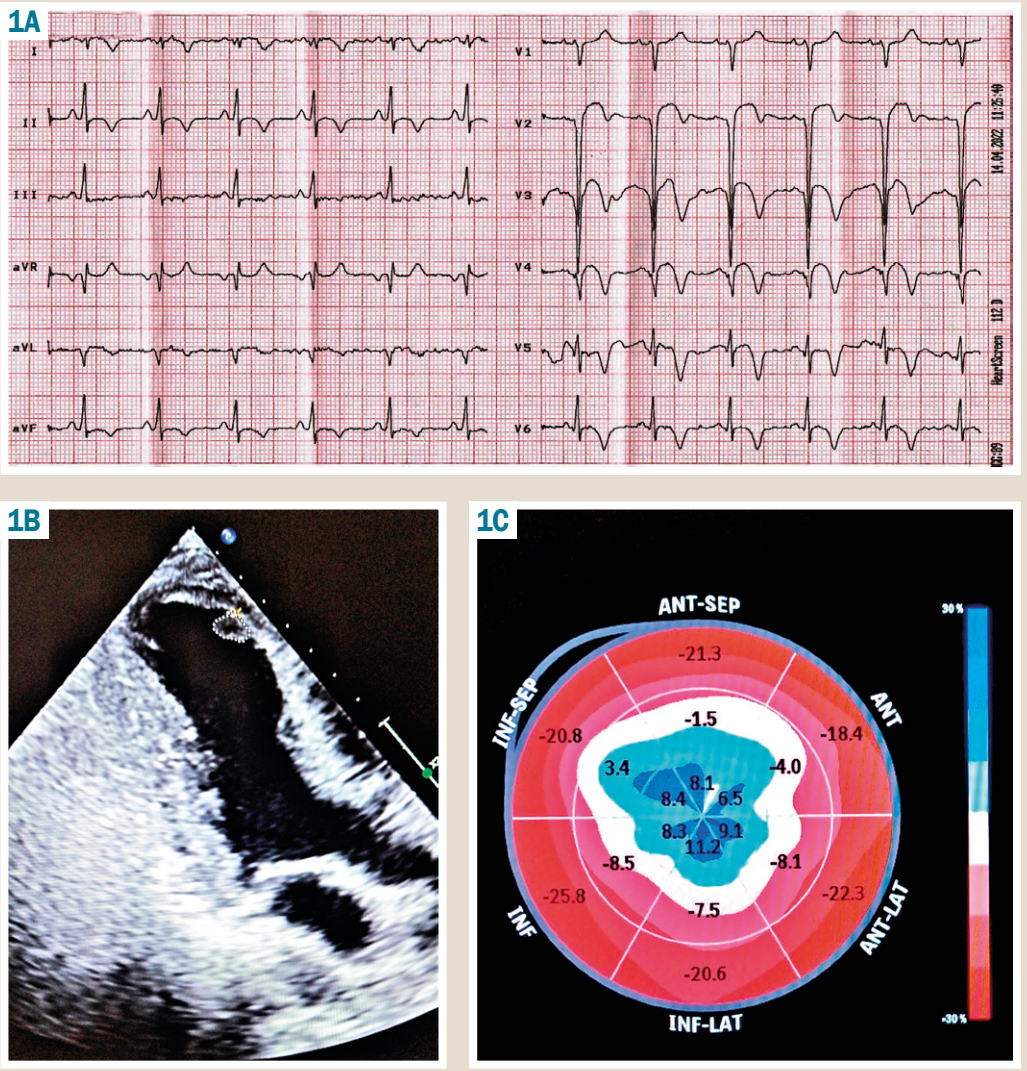



**Fig. 1.** Data of instrumental examinations of the patient (case 1).

**A:** ECG on day 16 after LAD ligation (Medical Heart Screen 112D, Innomed, Hungary).

**B:** EchoCG on day 15 after LAD ligation (EPIQ 5G, Philips Ultrasound Inc., USA) Image of the LV in 2D mode, LV aneurysm is located septoapically, the dotted line marks the parietal thrombus.

**C:** 2D speckle tracking echocardiography (EPIQ 5G, Philips Ultrasound Inc., USA), the bull's eye plot shows the regional value of circumferential strain for 17 segments demonstrating obvious signs of septoapical LV dyskinesis and proving the presence of aneurism in this site.

ST segment elevation remained in leads $V_{2-4}$ (QS graphics) on the ECG on the 16th day after LAD ligation, typical for a septoapical LV aneurysm (*Fig. 1*), the presence of which was confirmed by the results of CT and echoCG.

After 2 weeks, the patient was discharged with recommendations for the treatment of heart failure (LV ejection fraction (EF) before discharge was 47 %), follow-up by a cardiologist, antithrombotic/antiplatelet therapy as well as rehabilitation programs associated with the combined injury.

## Clinical case 2

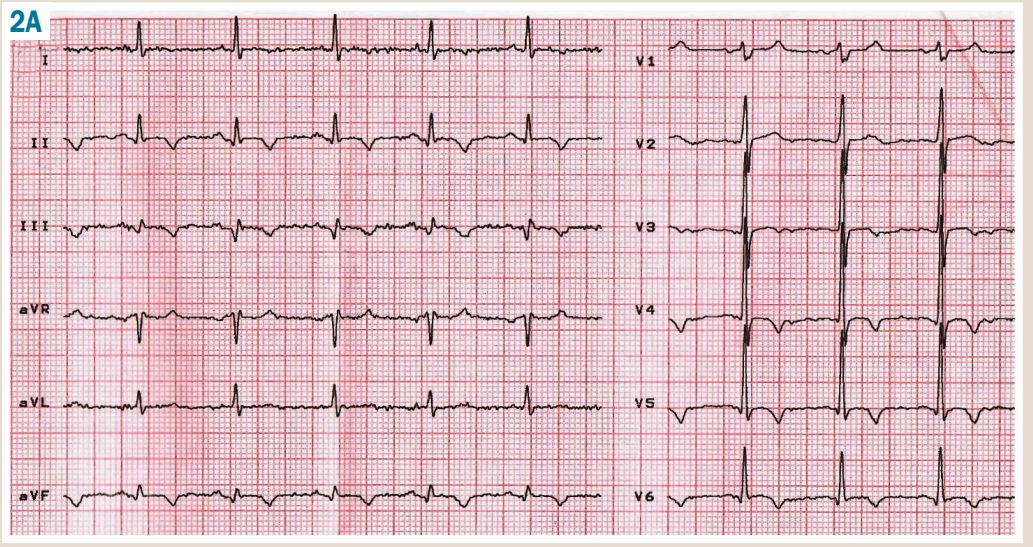
Another mechanism for the development of myocardial necrosis occurred in our next 49-year-old patient, male, who received a gunshot blind shrapnel penetrating wound to the right half of the chest on March 13, 2022. The patient was hospitalized to the nearest regional hospital, and then transferred to a military hospital, where he underwent PST of wounds, anterior right thoracotomy, suturing of the wounds of the right lung, drainage of the right pleural cavity. He received anesthesia with narcotic analgesics and transfusion of erythrocyte mass as a part of comprehensive treatment of his severe injury and posthemorrhagic anemia (hemoglobin level – 95 g/L, red blood cells – 3.1 × $10^{12}$/L). After his clinical condition stabilization, the patient was transferred to a specialized stage of medical care – to the Clinic of Thoracic Surgery of the National Military Medical Clinical Center "Main Military Clinical Hospital" (NMMCC "MMCH") on April 5, 2022.

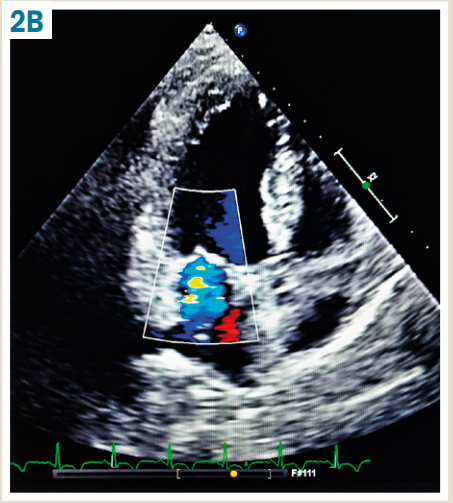
ECG registration revealed signs of myocardial necrosis (*Fig. 2*) in the form of a pathological Q wave in leads III and aVF (Qr graphics) and subendocardial ischemia in both apex and lateral wall of LV (presence of negative T waves in leads $V_{3-6}$).

EchoCG showed the presence of dyskinesia of the mid inferior LV segment, hypokinesis of the apex and mid septal segments together with slightly increased density of myocardium in several LV segments (*Fig. 2*). LV contractility was not reduced (LV EF 51 %).

The results of coronary angiography performed on April 8, 2022 (the right radial artery was punctured, the left and right coronary arteries were selectively catheterized) showed no obstructive changes (CAD-RADS score 0).

The patient was diagnosed with mine-explosive injury (03/13/2022), gunshot blind shrapnel penetrating wound



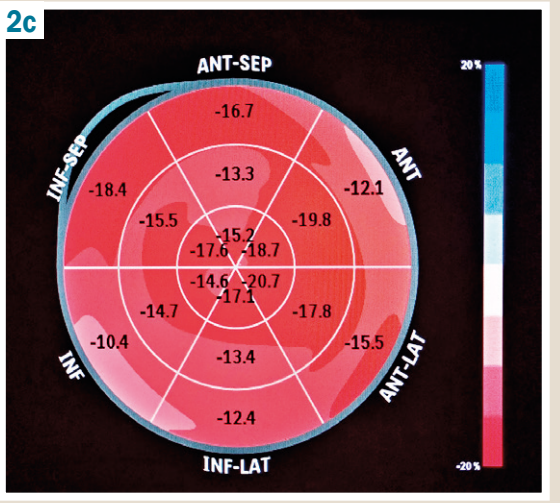




**Fig. 2.** Data of instrumental examinations of the patient (case 2).

**A:** ECG after three weeks from combat trauma (Medical Heart Screen 112D, Innomed, Hungary).

**B:** Doppler-echoCG after three weeks from combat trauma (EPIQ 5G, Philips Ultrasound Inc., USA). 2D mode image of LV demonstrates mitral valve regurgitation and increased density of the basal anterolateral, basal & mid inferoseptal segments of myocardium.

**C:** 2D speckle tracking echocardiography (EPIQ 5G, Philips Ultrasound Inc., USA), the bull's eye plot shows the regional value of longitudinal strain for 17 segments demonstrating hypokinesis with the basal anteroseptal, inferior and inferolateral segments being most affected.

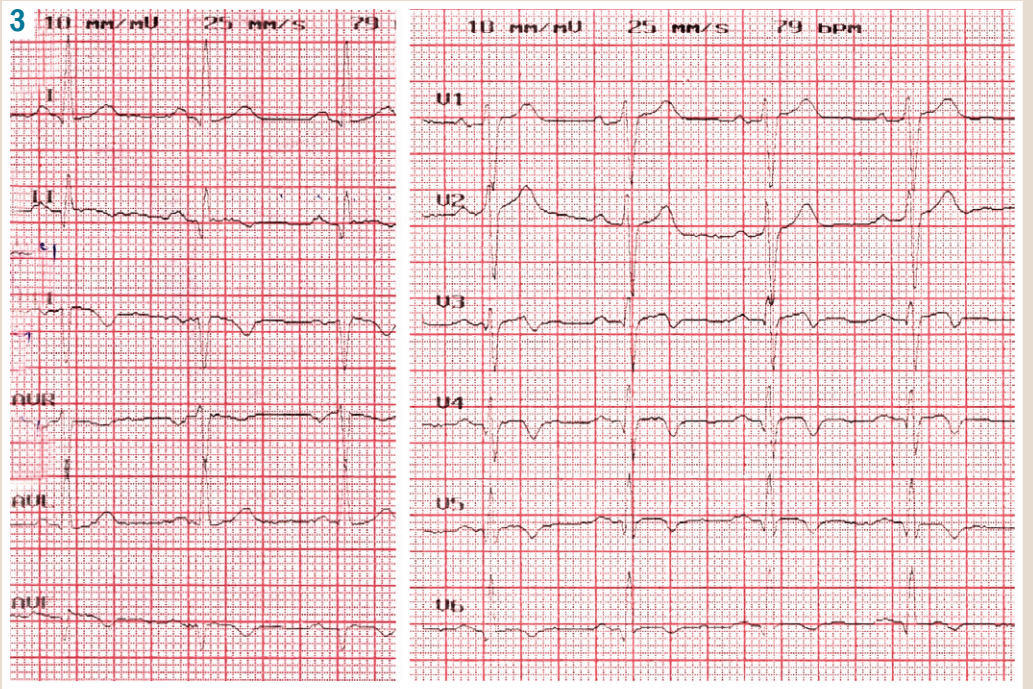



**Fig. 3.** ECG data of the patient (case 3) 5 months after combat injury, 2 months after anginal pain episode (Medical Heart Screen 112D, Innomed, Hungary).

(03/13/2022) of the right half of the chest with damage to the right lung, right-sided post-traumatic hemopneumothorax. Heart injury (03/13/2022): heart contusion with signs of myocardial necrosis – inferolateral LV Q-myocardial infarction according to ECG data. Coronary angiography 04/08/2022: CAD-RADS 0. Heart failure I stage with preserved LV systolic function (LV EF 51 %). Gunshot fracture of the right shoulder blade. PST of wounds of the right lung, drainage of the right pleural cavity (03/13/2022). Moderate posthemorrhagic anemia.

In this case, heart damage in the form of myocardial necrosis could be attributed to a severe degree of myocardial contusion according to the B. M. RuDusky classification as a result of myocardial tissue crushing and pathomorphological changes including foci of relaxation and dissociation of muscle fibers, intramural hemorrhages and microcirculation disorders with erythrocyte aggregation [7]. It was those changes that could cause the development of severe myocardial ischemia with the development of type 2 myocardial infarction.

## Clinical case 3

The following clinical case demonstrates another one variant of the development of type 2 myocardial infarction after a combat injury.

A 36-year-old patient, male, was admitted to the NMMCC "MMCH" for examination before the military medical commission for recognition of fitness for military service in October 2017.

On June 3, 2017, this patient received a mine injury, a ruptured fragmentary wound to the right shoulder with fractures and damage to the right brachial artery, and a gunshot wound to the left forearm while participating in hostilities in the Anti-terrorist operation zone in eastern Ukraine. He underwent PST of wounds, autovenous prosthesis of the right humeral artery, EFD of the right humerus was placed, fasciotomy of the muscular-fascial sheaths of the right forearm was performed.

Immersion metal osteosynthesis of the right humerus with bone autoplasty as well as plasticity of the median nerve and soft tissue defect of the right shoulder was performed on August 28, 2017 at the military hospital in Ulm (Germany).

Examination at the NMMCC "MMCH" showed signs of myocardial necrosis in the region of the inferior LV wall (ECG Qr graphics in leads III and aVF), aneurysm signs in leads $V_{3-6}$ (*Fig. 3*).

According to echoCG data, there was LV and left atrium dilatation, akinesis of the apex and apical segments of the interventricular septum, increased myocardial trabecularity with thrombotic layers in the region of the LV apex.

When clarifying the anamnesis, it was found that on the next day after surgery during treatment in Ulm, the patient had an episode of prolonged anginal pain, which was accompanied by general weakness and cold sweat. Shortness of breath appeared and persisted in the future during physical exertion (going up to the 3–4$^{th}$ floor). Medical records which were given to the patient in Germany at discharge were lost.

Electrocardiographic and echoCG changes became a reason to refer the patient for a consultation to the National Scientific Center "Institute of Cardiology named after M. D. Strazhesko", where coronary angiography revealed an intramural course (IC) in the region of the middle and distal third of the LAD with systolic compression up to 30–50 %.

In this case, it was likely that the causes of myocardial necrosis without atherosclerotic coronary artery disease were the presence of LAD anatomical feature in the region of the middle and distal third with systolic compression up to 50 % and sinus tachycardia (according to ECG Holter monitoring – sinus tachycardia with an average heart rate of 95 beats per 1 min, mean heart rate at the active period – 100 beats per 1 min, maximum heart rate during the day – 145 beats per 1 min), indicating a pronounced predominance of the sympathetic nervous system tone. Although the symptoms of ischemia are relatively rare for such condition as IC, severe sympathicotonia with tachycardia, increased physical activity, and LV hypertrophy may result in myocardial infarction in patients with this abnormality [8].

## Discussion

In all 3 clinical cases presented, young and middle-aged patients were diagnosed with myocardial infarction in accordance with the Fourth Universal Definition. In all these cases, there was no atherosclerotic lesion of the coronary vessels, and a type 2 myocardial infarction was assumed due to acute myocardial ischemia associated with: ligation of the coronary artery and severe anemia (case 1); microcirculation disorders in the area of myocardial contusion and moderate anemia (case 2): LAD IC and severe sympathicotonia with tachycardia (case 3). So, all these patients had signs of myocardial necrosis after combat trauma of the chest and heart, and therefore the question arose of the preference for encoding such conditions through ICD-10 as S26 (injury of heart), or, in some situations, as S25 (injury of blood vessels of thorax). In this way, the developed pathology will be clearly associated with the combat trauma, and treatment of such patients will not be tied to the current Unified Protocol for the Management of Patients with ST-segment Elevation Acute Coronary Syndrome [9]. The current recommendations of the European Society of Cardiology [10] after the adoption of the 4$^{th}$ Universal Definition of Myocardial Infarction have not been revised and do not consider special approaches to the treatment of patients with myocardial necrosis related to type 2 myocardial infarction. In the presented cases, the application of the recommendations regarding, for example, use of statins, does not seem appropriate.

In the first two cases, clinicians had questions related to the management of the patient, starting from the diagnosis (is that possible to diagnose the myocardial infarction without CAD?) and ending with recommendations at discharge (according to the recommendations for acute coronary syndromes, statins and aspirin should be prescribed). Special considerations were applied to diagnosis since in these cases clinicians were more oriented to the ECG data, clinical symptoms and signs. The main criterion for myocardial infarction – an increase in the blood levels of troponins – in these cases could be affected by a combined injury with significant damage to various tissues and organs, including the lung. So, it is known that acute myocardial injury is relatively common in COVID-19, especially in case

of its severe course, but the diagnostic role of troponins in confirming myocardial necrosis is considered less convincing in conditions of massive lung injury, cytokine storm and expression of angiotensin-converting enzyme 2 as a consequence of SARS-CoV-2 infection [11,12]. The position of the European Society of Cardiology in this regard is that an increase in the blood levels of troponins both slight (2–3 times the upper limit of normal) and more significant (more than 5 times the upper limit of normal) in the absence of other signs of myocardial ischemia does not require initiation of interventions for the treatment of type 1 myocardial infarction and, most likely, is associated with acute injury/stress as a result of the underlying disease [12].

In the third clinical case, myocardial damage was associated with the anatomical features of the coronary artery course. According to the literature, coronary artery IC (tunneled coronary artery, diving coronary artery) is the passage of the coronary artery in the myocardium under the "myocardial bridge", is a fairly common variant of the coronary artery passage. Information regarding the prevalence of coronary artery IC in the population differs significantly, although these differences are more likely related to the method of its diagnosis. It can be detected by coronary angiography in 2–6 %, by CT angiography – in 19.0–22.5 %, by intravascular ultrasound – in 23 % of patients [13–16]. According to autopsy data, IC of the coronary artery is found in 33–42 % of cases [13,17].

IC was considered as a benign deviation in the coronary artery development, which is usually asymptomatic. In a study with 334 participants, there was not found any relationship between coronary artery IC and the risk of cardiovascular death or myocardial infarction [18]. This was explained by the fact that about 85 % of the coronary blood flow occurs during diastole, thus, the loss of 15 % during systolic compression of the coronary artery was considered not so significant [18]. Later studies showed the variability of this proportion depending on the depth of the tunnel fragment, its length, the tone of the autonomic nervous system (high sympathetic tone results in an increase in heart rate, decrease in the time of diastolic perfusion, and slowdown in relaxation after contraction) [19,20]. Recently, the relationship between IC and the atherosclerotic process of the coronary artery has been actively studied. A number of factors have been proven to influence atherogenesis in the coronary artery in the presence of IC: the age of a patient, comorbid conditions resulting in the appearance of ischemia symptoms in previously asymptomatic patients (the location of the plaque proximal to the myocardial bridge, the presence of LV diastolic dysfunction, endothelial dysfunction, coronary vasospasm, and the state of the microvasculature) [21].

This series of cases demonstrates that clinical conditions of injured combatants are mostly unique and require special approach and understanding of the mechanism of myocardial damage development. Clinicians experience some issues related to diagnosis definitions and treatment of such patients, since it is obvious that Recommendations for the management of patients with acute coronary syndrome with/without ST segment elevation are not applicable in these situations.

One of the first studies assessing the possibility of developing heart damage in injured with blunt chest trauma, based on data from 280 patients, concluded that myocardial contusion occurred in 13 % of cases with blunt chest trauma [22]. According to the results of this study conducted before implementation of troponins for the diagnosis of myocardial infarction, the most useful data for detecting myocardial contusion were ECG data and monitoring of the activity of the creatine phosphokinase MB-fraction (every 8 hours for 48 hours), whereas X-ray and CT did not provide meaningful information about myocardial contusion, but showed other chest injuries [22].

An analysis of the results of a 10-year retrospective cohort study showed [23] that the best diagnostic approaches to identify patients with myocardial contusion after blunt chest trauma were ECG and blood levels of myocardial necrosis biomarkers (the sensitivity of the methods was 59 % for troponin T, 77 % – for high-sensitive troponin; the specificity of the methods was 63 % for MB-fraction of creatine phosphokinase and 100 % – for troponin T). In this study, chest X-ray, chest CT, ECG, and echoCG had significantly lower sensitivity. These authors also conducted a systematic review of 28 studies (7242 patients, of whom 14.5 % had myocardial contusion), the results of which were broadly consistent with previous data [23].

It is surprising that even in recent publications (2020–2021), such simple diagnostic methods as ECG and myocardial necrosis biomarkers are offered as methods for diagnosing myocardial contusions. Non-invasive imaging methods that can be used in the diagnosis of myocardial injury/infarction (echoCG, scintigraphy, CT, magnetic resonance imaging, etc.) allow the detection of local defects in contractility and non-viable myocardial zones and can confirm an acutely developed condition only in the presence of increased blood levels of myocardial necrosis biomarkers [24,25], since impaired local myocardial contractility may be associated with other, even non-cardiac, causes.

Based on the presented here cases and our previous scientific works [1,26], we can assume that the following circumstances should be considered when managing patients with combat trauma and acute heart damage, including myocardial necrosis:

1. Analgesic therapy, which can disguise the anginal pain clinic;
2. Worsening of myocardial ischemia in the presence of anemia;
3. Critical interpretation of increased troponin levels;
4. The possibility of clinical manifestation of the coronary artery anatomical features like IC in previously healthy young people.

Previously, we also showed that it is necessary to pay close attention to the assessment of the QT-interval duration on the ECG due to the use of certain antibiotics and antipsychotics in patients with combat injury [26].

## Conclusions

1. The described clinical cases demonstrate various mechanisms of myocardial necrosis development in injured with combat chest trauma and substantiate the need for an individual approach to such patients, both in terms of making a diagnosis and management tactics.

2. The obtained information substantiates the need for further study on the problem of acute heart injury in patients with combat chest trauma and the development of recommendations for their management, depending on the mechanism of myocardial injury.

**Prospects for further research.** The presented clinical cases substantiate the planning of clinical trials and the development of recommendations for the management of patients with acute myocardial injury (including myocardial necrosis) in patients with trauma to the heart and coronary arteries, depending on the mechanism of damage development.

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